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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,485	07/16/2003	Mike Mueckler	56029/41936	3332
21888	7590	10/31/2005	EXAMINER	
THOMPSON COBURN, LLP ONE US BANK PLAZA SUITE 3500 ST LOUIS, MO 63101			FERNANDEZ, SUSAN EMILY	
		ART UNIT	PAPER NUMBER	
		1651		

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

**Application No.**

10/621,485

**Applicant(s)**

MUECKLER ET AL.

**Examiner**

Susan E. Fernandez

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 October 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a)  The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
 b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2.  The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a)  They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b)  They raise the issue of new matter (see NOTE below);  
 (c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Attachment. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-15,22.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Attachment.  
 12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_  
 13.  Other: \_\_\_\_\_.

**ATTACHMENT TO ADVISORY ACTION**

The response filed October 4, 2005, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

The 10-4-05 amendment raises new issues under §112, second paragraph, with respect to claims 1-8, 30-32. As amended on 10-4-05, the claims are rendered indefinite by the recitation “ice cold”, and are confusing in that claim 32 does not logically depend from claim 1, as it is unclear how there can be both a presence and absence of insulin in step (b).

Additionally, the 10-4-05 amendment raises new issues of search and consideration since claims 1-8 and 30-32 previously did not require an ice cold buffer, the specific inclusion of components (i)-(iv) in a membrane fraction and components (i)-(v) in the cytoplasmic fraction as recited in claim 1, the autophosphorylation/phosphorylation/activation requirements of those components, or the PDK2 and PDK1 activities recited in claim 9.

Finally, the new language in the proposed amendment requires consultation of the specification to confirm support for the new language. Therefore, denial of entry of the proposed amendment is proper at this after-final stage of prosecution.

All of applicant’s argument has been fully considered but is not persuasive of error. The majority of applicant’s argument assumes entry of the non-entered amendment, and is thus directed to subject matter which is not presently entered into the claims. However, to the extent the applicant’s argument are applicable to the claims as pending, it does not demonstrate error for the reasons of record. With respect to the assertion that Wijkander et al. discloses only

obtaining from insulin-treated cells a protein kinase B that has been activated *in vivo*, note again that kinase activity was detected in a cytosol fraction and a mixture of membrane fraction and cytosol fraction which each constitute *in vitro* systems, thus protein kinase B had been activated *in vitro*. Moreover, the presently pending claims do not indicate that protein kinase B had not been activated in the insulin-responsive cell prior to obtaining membrane and cytoplasmic fractions. Claim 2 clearly results in the activation of protein kinase B in an insulin-responsive cell.

Additionally, the Cross et al. and Alessi et al. references are used to show that characteristics not disclosed in the Wijkander et al. reference are inherent in the 35 U.S.C. §102 rejections. Specifically, Cross et al. clearly discloses the inherent activity of Akt (PKB) in phosphorylating GSK3, and Alessi et al. clearly discloses the inherent requirement of phosphorylation of Ser473 and Thr30 for the full activation of PKB $\alpha$  *in vitro*. Thus, the rejections of record are maintained.

Since Wijkander et al., Alessi et al., and Cross et al. teach an *in vitro* method for activating protein kinase B with all the elements as required by presently pending parent claim 1, rejections based on the combination of these references with other references are appropriate. Thus, the rejections of claims 1-8 and 22 in view of Wijkander et al., Alessi et al., Cross et al., and Vanhaesebroeck, and claims 1-8 in view of Wijkander et al., Alessi et al., Cross et al., and Bauer et al., are maintained.

The Affidavit under 37 CFR §1.131 has been received and considered. Since the Affidavit presents evidence of possession (Exhibits 37 and 38) of the invention (recited in presently pending claims 9-15) prior to the July 23, 2002 date of the Hill et al. reference (Current

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Biology) the 103 rejections using Hill et al. (Current Biology) are withdrawn. However, re-evaluation of the Affidavit and Hill et al. (Current Biology) would be required if the 10-4-05 amendment or other amendments are entered in the future.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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